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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/137,059 | 08/20/1998 | BRIAN JOHNSTON | A-65200/WHD/ | 2454 |

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EXAMINER

SCHMIDT, MARY M

ART UNIT

PAPER NUMBER

1635

33

DATE MAILED: 02/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/137,059

Applicant(s)

JOHNSTON ET AL.

Examiner

Mary Schmidt

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-49 is/are pending in the application.
- 4a) Of the above claim(s) 27,29-31,33 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-26,28,32,34-36 and 38-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 30.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Upon entry of the Amendment filed 08/14/01, claims 24-49 are pending.
2. Applicant's election without traverse of the following species present in claims 23-26, 28, 32, 34-36 and 38-49: (I) **DNA (including ssDNA)** (instead of RNA, polypeptides, aptamers or metal ions) as the target molecule; (II) **hairpin** (instead of hammerhead) as the type of catalytic RNA; and (III) **not bound to the catalytic RNA** (instead of bound to the catalytic RNA or autocatalytic) as the location of the substrate in Paper No. 32, filed 12/06/01, is acknowledged.

Claims 27, 29-31, 33 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 32, filed 12/06/01. Specifically, claims 27, 29, 30 and 31 are drawn to species not elected in section (I); claim 33 is drawn to a species not elected in section (II); and claim 37 is drawn to a species not elected in section (III).

Claims 23-26, 28, 32, 34-36 and 38-49 are pending for consideration on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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4. Claims 23-26, 28, 32, 34-36 and 38-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the Official Action mailed 02/14/01.

Applicant's arguments filed 08/14/01 have been fully considered but they are not persuasive.

Specifically, it was argued in the Official Action mailed 02/14/01 that the specification as filed teaches Antisense-triplex-Ribozyme (ATR) molecules which have improved binding capacity over an Antisense-Triplex (AT) to the same "target". However, it is not clear how these types of constructs function to "act" on any other substrate (than the "target") as instantly claimed. As pointed out previously, on page 4 of the specification, it is taught that the "sense-antisense hybridization is unstable in the absence of the clasp molecule... the ends of the padlock DNA create a binding site for c-myc." And on page 3 it is taught that "the ball represents any of various ways for the ends of this molecule to interact following hybridization with the target with creation of at least one turn of helical interwinding.... In one embodiment, the ball comprises a hairpin ribozyme moiety." In the specific case of the ATR example, it is not clear that the ATR (specifically the R, the ribozyme) acts on a substrate other than the target which the ATR complex binds. And since the claim specifies a transition from a catalytically inactive to a

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catalytically active RNA, it is not clear what substrate the RNA is cleaving. The example of the c-myc binding does not qualify as a transition from a catalytically inactive to active RNA.

Applicants traverse the rejection by pointing to regions of the specification which teach prophetically the design of the RNA molecule, target and substrate compositions instantly claimed. However, Applicant does not address how the claimed RNA molecule goes from catalytically inactive to catalytically active, how the binding to c-myc is representative of binding to a substrate other than target, and further, how the various probe compositions act to bind a target (such as c-myc?) or not bind a target such that the catalytic RNA molecule may still become catalytically active. Furthermore, in view of the claim amendments, it is unclear what probes that RNA molecule is ligating such that the ligated probes may serve as a substrate for Qbeta replicase as newly claimed.

As such, in view of the lack of guidance in the specification as filed to make and use specific compositions which act as substrates other than a target molecule, one skilled in the art would necessarily practice "trial and error" experimentation to make such substrates. Although the art teaches probes which bind target nucleic acids, the art does not provide guidance on how to modify the teachings of the instant specification such that hairpin ribozymes may be used to ligate such probes for detection of another target molecule as instantly claimed. Without substantive guidance in either the specification or the art to make and use the claimed molecules together as claimed, one skilled in the art would necessarily practice undue experimentation to make and use the claimed invention.

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Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 23-26 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Bekkaoui et al. (U.S. Patent 6,136,533).

Bekkaoui et al. teach a method for detecting the presence of a target molecule in a composition suspected of containing said target molecule (abstract), said method comprising: contacting said composition (the target nucleic acid and single stranded nucleic acid probe (abstract) with an enzyme capable of cleaving the probe (ie. encompasses a catalytically inactive RNA molecule), wherein binding of said enzyme (ie. catalytically inactive RNA molecule) to said target molecule allows said enzyme to become catalytically active, and cleave a double-stranded target-probe complex at a scissile linkage (the substrate other than the target molecule, and bound to the target), wherein the action of the enzyme on the substrate is indicative of the presence of the target in said composition (see abstract and also col. 4, lines 52-66 for types of target nucleic acids).

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7. Claims 23-26, 32, 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Stefano et al. (U.S. Patent 5,472,840).

Stefano et al. teach a method for detecting the presence of a target molecule in a composition suspected of containing said target molecule (see col. 4, lines 17-61 for how to detect a DNA target), said method comprising: contacting said composition with a catalytically inactive RNA molecule which binds to said target molecule, wherein binding of said catalytically inactive RNA molecule to said target molecule allows said catalytically RNA molecule to become catalytically active toward a substrate other than the target molecule (see col 17 though col. 19 for a description of the types of target, probe and ribozyme reactions taught), wherein the action of the catalytically active RNA molecule on the substrate is indicative of the presence of said target molecule in said composition. (See also example 4, cols. 23-24 and col. 26, lines 28-30 for description of a capture probe captured on a solid support)

8. Claims 34-36 and 41-49 are free of the prior art since the art does not teach nor fairly suggest modification of the Bekkaoui et al. or Stefano et al. references for ligation of probes by the claimed methods, nor amplification of such substrates after ligation by Q beta replicase in the context of the instantly claimed methods.

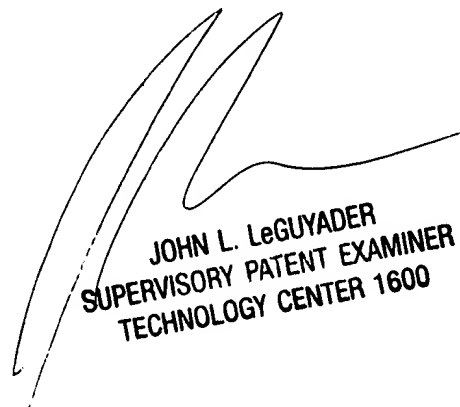
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
February 24, 2002



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